A Hypercellular Component of Glioblastoma Identified by High b-value Diffusion Weighted Imaging

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Glioblastomas (GBM) may receive inadequate radiation dose coverage, specially the nonenhanced hypercellular component, using post-Gd T1 weighted and T2 FLAIR images for radiation target definition. A mixture of edema, microvascular leakage, tumor cells and normal tissue in a single image result in an unpredictable value on diffusion images using a conventional b-value of 1000 s/mm² or less. This study aimed to develop a technique to identify the hypercellular components of GBM by using high b-value diffusion weighted imaging (DWI) to suppress fluid, edema, microvascular leakage and even normal tissue to an extent. The hypercellular volume (HCV) of the tumor was evaluated for radiation dose coverage and prediction of progression-free survival (PFS).

Forty patients with newly diagnosed GBM underwent chemoradiotherapy post-resection/biopsy. The target definition was based upon conventional MRI and RT planning followed standard guidelines. Pre-RT DWI was acquired with b-values of 0, 1000, and 3000 s/mm². A HCV was defined on the DWI with b=3000 s/mm² by a threshold obtained from normal tissue. The nonenhanced HCV was delineated by comparing to the Gd-enhanced gross tumor volume (GTV-Gd) on T1-weighted images. Radiation coverage of the HCV was evaluated by the 95% prescribed dose-volume (95%PDV) of the planned dose distribution. Association between HCV and PFS or other clinical covariates were assessed using univariate proportional hazards regression models.

For the first 21 patients with a minimum follow-up of 18 months, the HCVs varied 0.58-67 cc (median: 9.8cc), 7 times smaller than the FLAIR-defined CTV. The non-enhanced HCV was 0.15-60 cc (median: 2.5cc). However, incomplete dose coverage of the HCV was seen in 14 patients, in whom 6 had at least 1-cc HCV missed by the 95%PDV (range: 1.01-25.4cc). Of the 21 patients, 15 had progressed, 5 patients earlier within 6 months post-RT, and 10 patients >6 months post-RT. HCV and nonenhanced HCV were significant negative predictors for PFS (p<0.002 and p<0.01, respectively). The component of the HCV that was not covered by the 95%PDV was a significant negative predictor for PFS (p<0.05). The proportion of pre-RT HCVs that overlapped with recurrent Gd-enhanced tumor volume was 78% (range: 65-89%) for the 5 earlier progressors, and 53% (range: 0-85%) for the later progressors.

The HCV identified by high b-value DWI most likely represents an aggressive component of the tumor, and analysis of the data from the whole cohort is in progress. Pathological validation is on-going. Post-Gd T1 weighted images (a qualitative measure of vascular leakage) and T2 FLAIR images (influenced by edema) are not adequate for radiation target definition of GBM. Selectively boosting the HCV component of GBM will be tested in a prospective clinical trial.

Keywords: glioblastoma, high b-value diffusion weighted imaging, radiation
A least absolute shrinkage and selection operator (LASSO) method was used for feature selection. Model performance was evaluated using Harrell’s concordance-index (c-index). Fitted model included sum entropy (GLCM), high intensity large area emphasis (GLCM), volume with a minimum relative intensity of 60% of the maximum SUV - AVR60% (VH), grey level non-uniformity and long run emphasis (RLGL) and volume (shape) - Table 1. Internal performance of the model was 0.64 (p<0.01), while externally it achieved a performance of 0.61 (p = 0.05) and 0.58 (0.20), with no further calibration done. Maximum and mean SUV had a univariable performance in the training data of 0.51 and 0.55, respectively.

The reduced accuracy of the model validation can be associated with dissimilarities among data, particularly the different time and delivered dose of the second scan. Nevertheless, we do see benefit on a timely assessment of response to radiotherapy using the described imaging analysis, particularly when compared with the limited capacity of humans to infer accurate predictions and risk groups identification (5). From the Radiomics analysis one can optimally benefit from early response metrics based on changes in metabolism measured with FDG-PET, even before anatomic changes become noticeable, while treatment can still be adapted.

We developed and validated a predictive model on the percentage variation of Radiomics features, the so-called “Delta Radiomics” concept, from repeated FDG-PET scans of NSCLC patients.

**References:**


43 Proton scattering radiography using an emulsion detector: a feasibility study

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Purpose: Proton radiography is an imaging technique in proton therapy giving direct information on the density of the tissues, a useful tool to enhance the precision of proton therapy. It is usually performed as a proton range radiography by measuring the position and the residual range of the protons after the target. The properties of the traversed materials are directly related to multiple scattering so that it is possible to obtain an image through the assessment of the proton angular distribution. This work aims at studying the possibility of performing proton scattering radiography using only one nuclear emulsion film.

Materials and methods: Nuclear emulsion films allow for high-precision tracking of charged particles and, in particular, for reconstructing their angular distribution with a resolution of the order of 1 mrad. Specific detectors for medical applications can be built by interposing double-sided emulsion films with tissue equivalent materials, as it was done for proton range radiography [1] and to study the halo of a proton pencil beam [2]. In the present study, a detector composed by only one emulsion film was exposed to a 138 MeV proton pencil beam at the Gantry 1 at PSI. Two phantoms were placed in front of the detector: the “step” phantom consisted of two different thicknesses of PMMA (3 and 4 cm, respectively); the “rod” phantom had a total thickness of 4.5 cm and contained five aluminum rods (5 × 5 mm² section) positioned at different depths in a PMMA structure. Following the chemical development and the automatic microscopic scanning of the emulsion film, proton tracks were identified and their angular distribution reconstructed.

Results: The RMS of the scattering angle was measured for different segmentations of the emulsion film. Areas were chosen as strips parallel to the direction of the step or of the rods, for the first and the second phantom, respectively. To evaluate the resolution, strips of different sizes were considered. As shown in figure 1 (left), the step is clearly identified as a sharp drop of the RMS of the scattering angle. The signal due to the rods is visible as an enhancement of the RMS corresponding to their positions. The rod located nearest to the detector shows a sharper peak where the farther one appears broader due to the larger distance travelled by the protons. While the contrast for the step phantom is found to basically the same for range and scattering proton radiography, the signal due to the rods is more evident with respect to what was obtained with proton range radiography [1]. These preliminary results suggest that atomic number plays a fundamental role to increase the contrast of the image.

Conclusions: A feasibility study of proton scattering radiography with a new method based on a single emulsion detector has been performed. The first preliminary results are promising and further studies are under way encompassing in particular Monte Carlo simulations.

Keywords: Proton radiography, proton therapy, nuclear emulsion detectors

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